Sleep Medicine 16 (2015) 59–66

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Sleep apnea and periodic leg movements in the first year after spinal cord injury ☆

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A R T I C L E I N F O

Article history:
Received 2 April 2014
Received in revised form 8 July 2014
Accepted 14 July 2014
Available online 7 October 2014

Keywords:
Sleep-disordered breathing
Periodic leg movements
Spinal cord injury
Hypoventilation
Obstructive sleep apnea
Tetraplegia
Paraplegia

A B S T R A C T

Background: Sleep disturbances are frequently reported by patients with spinal cord injury (SCI). Studies have shown an increased incidence of sleep-disordered breathing (SDB) and periodic leg movements during sleep (PLMS) in people with stable long-term SCI.
Methods: This was a prospective observational study in order to evaluate the features and possible predisposing factors of SDB and PLMS in a heterogenic population of consecutive SCI patients admitted at the Spinal Unit of the Niguarda Hospital within the first year after injury. Each patient underwent a clinical assessment, full polysomnography, and arterial blood gas analysis before and immediately after sleep. Multiple logistic regressions were applied in order to evaluate factors associated with SDB and PLMS.
Results: Thirty-five (15 tetraplegic and 20 paraplegic) patients were enrolled. Nine patients (25.7%) had an obstructive SDB and 10 (28.6%) had PLMS. The frequency of SDB was higher in tetraplegic with respect to paraplegic patients (Wald statistic: 7.71; $P = 0.0055$), whereas PLMs were significantly more frequent in patients with an incomplete motor lesion than in subjects with a complete motor lesion (Wald statistic: 6.14; $P = 0.013$).
Conclusion: This study confirms a high frequency of SDB and PLMS in SCI patients in the first year following injury. Independently from possible sub-acute and chronic clinical variables, the level and the completeness of the spinal cord lesion are the main factors associated respectively with an early development of SDB and PLMS.

1. Introduction

Dysfunctional sleep is frequently reported in patients with spinal cord injury (SCI) [1,2]. This is partly related to neurogenic pain, spasticity, and other medical conditions resulting from the spinal cord lesions and also to specific sleep-related disorders, such as sleep-disordered breathing (SDB) or periodic leg movements during sleep (PLMS) [3,4].

Different studies have shown an increased incidence of SDB in people with SCI [3,5–11]. Indeed, despite differences in methodology and patient selection (low representation of women and paraplegic patients), the medical literature indicates a prevalence of SDB in patients with SCI that is at least twice the reported prevalence in the general population [7,8,10]. Moreover, among SCI patients, subjects with cervical lesions seem to be more prone to develop SDB [12]; and, within SDB, obstructive sleep apnea rather than central sleep apnea predominates [8,13]. However, the pathogenic mechanisms that cause SDB in SCI patients are still unclear. In particular, there are no data about the onset time of SDB because the majority of these studies have been conducted several years after injury [5–8,10], whereas only two recent studies investigated the SDB during the acute phase of SCI [9,11].

Moreover, limited data are available on the presence of PLMS in SCI. Indeed, available studies consist only of small case series that included stable long-term SCI patients [14–17].

The aim of our study was to evaluate the features and possible factors associated with SDB and PLMS in a heterogenic population of SCI patients (paraplegic and tetraplegic patients with complete or incomplete lesions) during the first year after injury.

☆ An editorial on this original article was published in Sleep Medicine November 2014 Volume 15, Issue 11.

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http://dx.doi.org/10.1016/j.sleep.2014.07.019
1389-9457/

2. Methods

2.1. Study design

This was a prospective observational study. A consecutive series of patients admitted at the Spinal Unit of the Niguarda Hospital, Milan, Italy, was analyzed during the first year after SCI from September 2010 to December 2011. Exclusion criteria were inability to give informed consent, significant head injury (amnesia >24 h post injury, evidence of cerebral contusion on computed tomography), presence of tracheostomy at time of enrollment, ventilator dependent at time of enrollment, and other respiratory problems (chest infection, pneumothorax, hemothorax, effusion, intercostal catheter).

Each patient underwent a clinical assessment and full polysomnography.

Clinical assessments included body mass index (BMI, body weight/height squared, kg/m^2), neck circumference, oral anatomy according to Mallampati et al. [18] and medication usage.

The location of the lesion and its extent were assessed in each patient by magnetic resonance imaging, evoked potential, and electromyography. Motor and sensory examinations were performed and all patients were classified using the American Spinal Injury Association (ASIA) impairment scale A–D [19]. A visual analogic scale (VAS) was used to assess the degree of daytime sleepiness. The Berlin Questionnaire [20] was used in order to evaluate possible presence of SBD preceding the injury (written permission had been obtained for its use).

A standard overnight full polysomnography was performed on the ward in an attended setting (AURA®; PSG Ambulatory Systems GRASS Technologies, Warwick, RI, USA). In accordance with standard criteria [21], the recording included: electroencephalography (at least three channels), bilateral electro-oculography, chin and tibial electromyography, electrocardiography, oronasal airflow, chest and abdominal effort (recorded using respiratory inductance plethysmography), pulse oximetry, and sensor of body position. All studies were manually reviewed by a medical doctor expert in sleep medicine, certified by the Italian Association of Sleep Medicine. Sleep was staged and respiratory and motor events were scored according to standard criteria [21].

The SDB was classified as mild if the apnea–hypopnea index (AHI, number of respiratory events per hour of sleep) was between 5 and 15, moderate if the AHI was between 15 and 30, and severe if the AHI was >30. All patients underwent arterial blood gas analysis before and immediately after sleep in order to assess the presence of hypoventilation during sleep [21].

The periodic leg movements index (PLMI) was defined as the number of PLM per hour of sleep.

LM was not scored if it occurred during a period from 0.5 s preceding an apnea or hypopnea to 0.5 s following an apnea or hypopnea [21]. Consistent with the ICSD-2 criteria [22], PLMI >15 was used as the cut-off criterion for the presence of PLMS.

All patients gave written informed consent before enrollment. The study was approved by the ethics committee of the Niguarda Hospital (Milan, Italy; record no. 991).

2.2. Statistical analysis

For descriptive statistics, clinical and polysomnographic data were summarized for tetraplegic and paraplegic patients (Tables 1 and 2), for patients with and without SDB (Table 3), and patients with and without PLMS (Table 4). A comparison between the two groups was independently performed for each variable by applying an appropriate test: the parametric *t*-test for interval variables with approximately normal distribution (after log or logit transformation when required), the Mann–Whitney *U*-test for interval variables with clearly non-normal distribution, and the Fisher exact test for dichotomic variables.

In order to evaluate factors associated with SDB, the multiple logistic regression with SDB classification (absent/mild/moderate/severe) was applied as ordinal dependent variable, with the following as independent variables (five categorical and four interval variables): gender (M/F), lesion site (cervical/other), lesion completeness (complete/incomplete), Mallampati score >2, muscle relaxant drugs use, age, BMI, neck circumference, and time elapsed since injury event. Forward stepwise selection was applied in order to identify significant factors.

The same multiple logistic regression method was applied to identify factors associated with presence of PLMS (PLMI >15). In this case, five categorical variables (gender, lesion site, lesion completeness, use of antidepressant, and use of antiepileptic drugs) and two interval variables (age and time since the injury event) were considered and selected by forward stepwise analysis.

Statistical analyses were performed with the Statistica version 10 software package (StatSoft, Inc., Tulsa, OK, USA).

Table 1
Demographic features of the studied population.

	Total ($n = 35$)	Tetraplegic ($n = 15$)	Paraplegic ($n = 20$)
Age (years)[a]	38.2 (16.3)	43.7 (18.7)	34.1 (13.3)
Male/female	29/6	13/2	16/4
BMI (kg/m^2)[a]	23 (2.8)	23.6 (2.3)	22.6 (3.1)
Neck circumference (cm)[a]	36.7 (3.3)	37.9 (3.1)	35.9 (3.4)
Completeness of SCI (ASIA scale)			
A	17	4	13
B	4	2	2
C	12	8	4
D	2	1	1
Time since injury (days)[a]	77 (68)	78.7 (74.6)	69.8 (57.8)
Daytime sleepiness (VAS ≥5)	5	2	3
Drugs			
Benzodiazepines	24	9	15
Opioids	14	8	6
Serotoninergic antidepressants	17	7	10
Tricyclic antidepressants	4	2	2
Muscle relaxants	12	7	5

Abbreviations: BMI, body mass index; SCI, spinal cord injury; ASIA, American Spinal Injury Association; VAS, visual analogic scale.
[a] Mean (standard deviation).
General clinical features were not significantly different in tetraplegic patients with respect to paraplegic ones.

Table 2
Polysomnographic parameters of the studied population.

	Total ($n = 35$)	Tetraplegic ($n = 15$)	Paraplegic ($n = 20$)
TST (min)[a]	458.4 (91.9)	450.8 (91.5)	464 (94.2)
N1 (% of TST)[a]	13.7 (9.1)	15.8 (10.1)	12.1 (8.2)
N2 (% of TST)[a]	49.1 (12.1)	49.7 (12.6)	47.5 (12.8)
N3 (% of TST)[a]	21.8 (11.7)	19.4 (14.7)	23.6 (8.8)
REM (% of TST)[a]	15.5 (7.8)	15.1 (8.1)	15.7 (7.9)
AHI[a]	6.7 (14)	13.9 (19.4)	1.4 (1.7)*
ODI[a]	8.2 (16.2)	16 (22.4)	2.4 (4)**
AHI >5	9	8	1***
PLM index[a]	25.6 (44.4)	31.4 (46.4)	23.8 (62)
PLMS (PLM index >15)	10	6	4

Abbreviations: TST, total sleep time; N1, sleep stage N1; N2, sleep stage N2; N3, sleep stage N3; REM, rapid eye movement sleep; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; PLMS, periodic leg movements in sleep.
[a] Mean (standard deviation).
AHI and ODI were significantly higher in tetraplegic patients: *Mann-Whitney *U*-test, $P = 0.013$; **Mann-Whitney *U*-test, $P = 0.016$; ***Fisher's exact test, $P = 0.0019$.

Table 3
Demographic features and polysomnographic parameters of the studied population, comparing patients with and without sleep-disordered breathing (SDB).

	Total ($n = 35$)	SDB patients ($n = 9$)	Non-SDB patients ($n = 26$)
Age (years)[a]	38.2 (16.3)	46.3 (18.6)	35.4 (14.8)
Male/female	29/6	8/1	21/5
BMI (kg/m^2)[a]	23 (2.8)	24.2 (2.5)	22.6 (2.8)
Neck circumference (cm)[a]	36.7 (3.3)	38.2 (3.7)	36.2 (3.1)
Lesion site	15 (42.9%)	8 (88.9%)	7 (26.9%)
Cervical	19 (54.3%)	1 (11.1%)	18 (69.2%)
Thoracic	1 (2.9%)	0	1 (3.9%)
Lumbar			
Completeness of SCI (ASIA scale)			
A	17 (48.6%)	2 (22.2%)	15 (57.7%)
B	4 (11.4%)	2 (22.2%)	2 (7.7%)
C	12 (34.3%)	5 (55.5%)	7 (26.9%)
D	2 (5.7%)	0	2 (7.7%)
Time since injury (days)[a]	77 (68)	89 (95)	72.4 (58)
Daytime sleepiness (VAS ≥5)	5 (14.3%)	2 (22.2%)	3 (11.5%)
Drugs			
Benzodiazepines	24 (68.6%)	6 (66.7%)	18 (69.2%)
Opioids	14 (40.0%)	4 (44.4%)	10 (38.5%)
Serotoninergic antidepressants	17 (48.6%)	4 (44.4%)	13 (50.0%)
Tricyclic antidepressants	4 (11.4%)	0	4 (15.4%)
Muscle relaxants	12 (34.28%)	3 (33.3%)	9 (34.62%)
TST (min)[a]	458.4 (91.9)	447.2 (60.9)	462.2 (100.5)
N1 (% of TST)[a]	13.7 (9.1)	19.5 (11.1)	11.7 (7.6)*
N2 (% of TST)[a]	49.1 (12.1)	47.8 (10.2)	49.5 (12.8)
N3 (% of TST)[a]	21.8 (11.7)	14.9 (11.5)	24.2 (11)**
REM (% of TST)[a]	15.5 (7.8)	17.8 (8.8)	14.6 (7.5)
PLM index[a]	25.6 (44.4)	35.5 (44.4)	20.8 (57.7)
PLMS (PLM index >15)	10 (28.6%)	5 (55.5%)	5 (19.2%)

Abbreviations: SCI, spinal cord injury; BMI, body mass index; ASIA, American Spinal Injury Association; VAS, visual analogic scale; TST, total sleep time; N1, sleep stage N1; N2, sleep stage N2; N3, sleep stage N3; REM, rapid eye movement sleep; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; PLMS, periodic leg movements in sleep.
[a] Mean (standard deviation).
SDB patients had a statistically significantly higher amount of N1 [*t-test, $t(33) = 2.495$; $P = 0.018$] and lower amount of N3 [**t-test, $t(33) = -2.688$; $P = 0.011$].

3. Results

Between September 2010 and December 2011, 65 patients were admitted at the Spinal Unit of the Niguarda Hospital during the first year after SCI. Thirty-five patients were enrolled. Their demographic features are summarized in Table 1. The mean age of patients was 38.2 years [standard deviation (SD), 16.3]; 29 subjects (82.9%) were males, six (17.1%) were females. The mean BMI was 23 kg/m^2 (SD, 2.8); six patients were overweight (BMI >25 kg/m^2), one of whom was moderately obese (30.1 kg/m^2). The mean value of neck circumference was 36.7 cm (SD, 3.3). Thirty-three patients had a Mallampati score of 1 or 2 and two subjects a Mallampati score of 3. Three patients were smokers.

Mean time since injury was 77 days (S.D. 68). Fifteen patients (42.8%) had a cervical lesion, 19 (54.3%) a thoracic lesion, and one (2.9%) a lumbar lesion. The lesion was complete (ASIA A) in 13 patients (37.1%), incomplete (ASIA B, C and D) in 22 (62.9%). All patients were without relevant comorbidities except one subject with a history of hypertension. After injury, the majority of patients were under polypharmacotherapy, including benzodiazepines, antidepressants, opioids, and muscle relaxants.

The Berlin Questionnaire did not reveal a high risk of SDB in any patients. Five patients complained daytime sleepiness (VAS score ≥5).

The polysomnographic findings are reported in Table 2. The proportion of rapid eye movement (REM) sleep was slightly reduced [23]. In particular, in 11 patients (31.4%) the percentage of REM sleep was less than 10% of total sleep time.

Nine patients (25.7%) had SDB. In all of them, the respiratory events were mostly obstructive in nature (Fig. 1A,B). The SDB was mild in four patients (44.4%), moderate in three (33.3%) and severe in two (22.2%). The mean of SpO_2 nadir was 89.0%; the mean minimum SpO_2 value was 80.9%. Among patients with SDB, six maintained the supine position throughout the night; in the three patients who changed body position, two of them had respiratory events mainly in supine position. Eleven out of the 35 patients had AHI ≥5 exclusively during REM sleep.

With respect to arterial blood gas analysis data, only one tetraplegic patient with mild SDB (AHI = 7.81; AHI in REM = 20.4) showed >10 mmHg increase in $PaCO_2$ immediately after waking in the morning by comparison with the awake value, suggesting the presence of sleep hypoventilation.

The mean PLMI was 24.4 (SD, 54.4). Ten patients (28.6%) had PLMS (Fig. 2A–C); among them five patients had PLMI >50. In eight patients, PLM persisted during REM sleep (Fig. 2C); in nine patients, PLM occurred also during wakefulness (Fig. 2A). In some patients, PLMS appeared only on one side for several minutes (Fig. 2B,C). However, in no patient was unilateral PLMS observed during the registration period.

3.1. Statistical analysis

General clinical features were not significantly different in tetraplegic patients with respect to paraplegic ones (Table 1). Considering polysomnographic data (Table 2), significant differences between tetraplegic and paraplegic patients were observed for SDB-related parameters: AHI and ODI were significantly higher in tetraplegic patients (Mann–Whitney U-test; AHI: adjusted $Z = 2.47$, $P = 0.013$; ODI: adjusted $Z = 2.42$, $P = 0.016$); 8/15 tetraplegic patients but only 1/20 paraplegic patients had AHI >5 (Fisher exact test: $P = 0.0019$).

SDB patients with respect to patients without SDB had a statistically significantly higher amount of N1 [*t-test, $t(33) = 2.495$; $P = 0.018$] and lower amount of N3 [**t-test, $t(33) = -2.688$; $P = 0.011$]

Table 4
Demographic features and polysomnographic parameters of the studied population, comparing patients with and without periodic leg movements (PLMS).

	Total ($n=35$)	Patients with PLMS ($n=10$)	Patients without PLMS ($n=25$)
Age (years)[a]	38.2 (16.3)	38 (23.2)	38.2 (13.2)
Male/female	29/6	9/1	20/5
BMI (kg/m^2)[a]	23 (2.8)	23.5 (1.9)	22.8 (3.1)
Neck circumference (cm)[a]	36.7 (3.3)	37.2 (3)	36.6 (3.6)
Lesion site			
Cervical	15 (42.9%)	6 (60.0%)	9 (36.0%)
Thoracic	19 (54.3%)	4 (40.0%)	15 (60.0%)
Lumbar	1 (2.9%)	0	1 (4.0%)
Completeness of SCI (ASIA scale)			
A	17 (48.6%)	1 (10.0%)	16 (64.0%)
B	4 (11.4%)	1 (10.0%)	3 (12.0%)
C	12 (34.3%)	7 (70.0%)	5 (20.0%)
D	2 (5.7%)	1 (10.0%)	1 (4.0%)
Time since injury (days)[a]	77 (68)	67.7 (82.5)	79.3 (63)
Daytime sleepiness (VAS ≥5)	5 (14.3%)	2	3 (12.0%)
Drugs			
Benzodiazepines	24 (68.6%)	6 (60.0%)	18 (72.0%)
Opioids	14 (40.0%)	4 (40.0%)	10 (40.0%)
Serotoninergic antidepressants	17 (48.6%)	5 (50.0%)	12 (48.0%)
Tricyclic antidepressants	4 (11.4%)	0	4 (16.0%)
Muscle relaxants	12 (34.3%)	4 (40.0%)	8 (32.0%)
TST (min)[a]	458.4 (91.9)	448 (77.7)	462.5 (98.2)
N1 (% of TST)[a]	13.7 (9.1)	16.5 (12.4)	12.6 (7.6)
N2 (% of TST)[a]	49.1 (12.1)	45.9 (5.7)	50.3 (13.7)
N3 (% of TST)[a]	21.8 (11.7)	18.7 (9.1)	23 (12.5)
REM (% of TST)[a]	15.5 (7.8)	18.9 (8.3)	14 (7.4)
AHI[a]	6.7 (14)	6.9 (7.8)	6.6 (16)
ODI[a]	8.2 (16.2)	9.5 (12.3)	7.7 (17.7)
AHI >5	9 (25.7%)	5 (50.0%)	4 (16.0%)

Abbreviations: BMI, body mass index; SCI, spinal cord injury; ASIA, American Spinal Injury Association; VAS, visual analogic scale; TST, total sleep time; N1, sleep stage N1; N2, sleep stage N2; N3, sleep stage N3; REM, rapid eye movement sleep; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; PLMS, periodic leg movements in sleep.
[a] Mean (standard deviation).

(Table 3). Clinical and polysomnographic features were not significantly different in patients with and without PLMS (Table 4).

As for SDB classification, multiple logistic regression confirmed the significant effect of lesion site (Wald statistic = 7.71; $P=0.0055$) and showed a weaker effect of BMI (Wald statistic = 5.14; $P=0.023$). No other independent variable showed any effect on SDB level. As the only obese patient had an AHI three standard deviations greater than the mean value of the remaining group, a further analysis was performed excluding him as outlier: BMI was no longer significant and the only significant factor was the lesion site (Wald statistic = 7.47; $P=0.0063$). Since SDB (AHI >5) was observed in 11/35 patients exclusively during REM sleep, further analysis was performed to individuate factors possibly associated with such a characteristic. Logistic regression with the same independent variables, but evaluating the probability of finding SDB only during REM sleep, indicated that such probability could increase with patient age (Wald statistic = 4.91; $P=0.027$) and lesion completeness: ASIA levels A and B (Wald statistic = 4.89; $P=0.027$).

The only factor significantly associated with the presence of PLMS was the lesion completeness (Wald statistic = 6.14; $P=0.013$). In particular, the presence of PLMS was much higher for incomplete lesions (ASIA C and D; Table 4).

4. Discussion

The main finding of our study is that, in the first year after SCI, the frequency of SDB is higher in tetraplegic with respect to paraplegic patients, whereas PLMS are significantly more frequent in patients with an incomplete motor lesion (ASIA C/D) than in subjects with a complete lesion (ASIA A/B).

Considering that the prevalence of SDB in the 30–49-year-old general population is about 10% in men and 3% in women [24], our data seem to suggest a higher prevalence of this sleep disorder (25.7%) in our SCI population. This confirms the observations from previous studies that enrolled between 10 and 53 SCI patients and showed an increased incidence of SDB, ranging from 9% to 68% [7,8,10] depending on the different recording methods and the selection of population. None of our patients had a high risk of SDB at the Berlin Questionnaire and they did not show the typical clinical features of SDB patients (except for a patient with BMI >30, who was excluded from statistical analysis as an outlier). This finding seems to suggest that the high prevalence of SDB in our population is related to the lesion per se rather than to a pre-injury condition. Moreover, considering that we analyzed patients within 10 months from the trauma (with 75% of patients enrolled in the first 2 months), SDB seems to develop early in a significant proportion of patients. Only two recent studies assessed the presence of SDB in the first year after SCI [9,11]. In particular, Berlowitz et al. [9] examined sleep breathing of SCI patients longitudinally during the first year post injury and found a prevalence of SDB of 60% at four weeks from injury that peaked at 83% at 13 weeks. This high prevalence could be explained by their selected population consisting of only tetraplegic patients. Indeed, our statistical analysis showed a significantly higher prevalence of SDB in patients with cervical lesions (53.3%) compared with paraplegic subjects (4.7%). Other studies, analyzing chronic SCI population [12], seem to confirm that tetraplegic patients are particularly prone to develop SDB. Several potential factors have been proposed to explain the pathophysiology of SDB in patients with cervical lesions [3,8,13]. These include respiratory muscle weakness and impaired diaphragm mobility (in patients with lesion of C5 and above); poor coordination

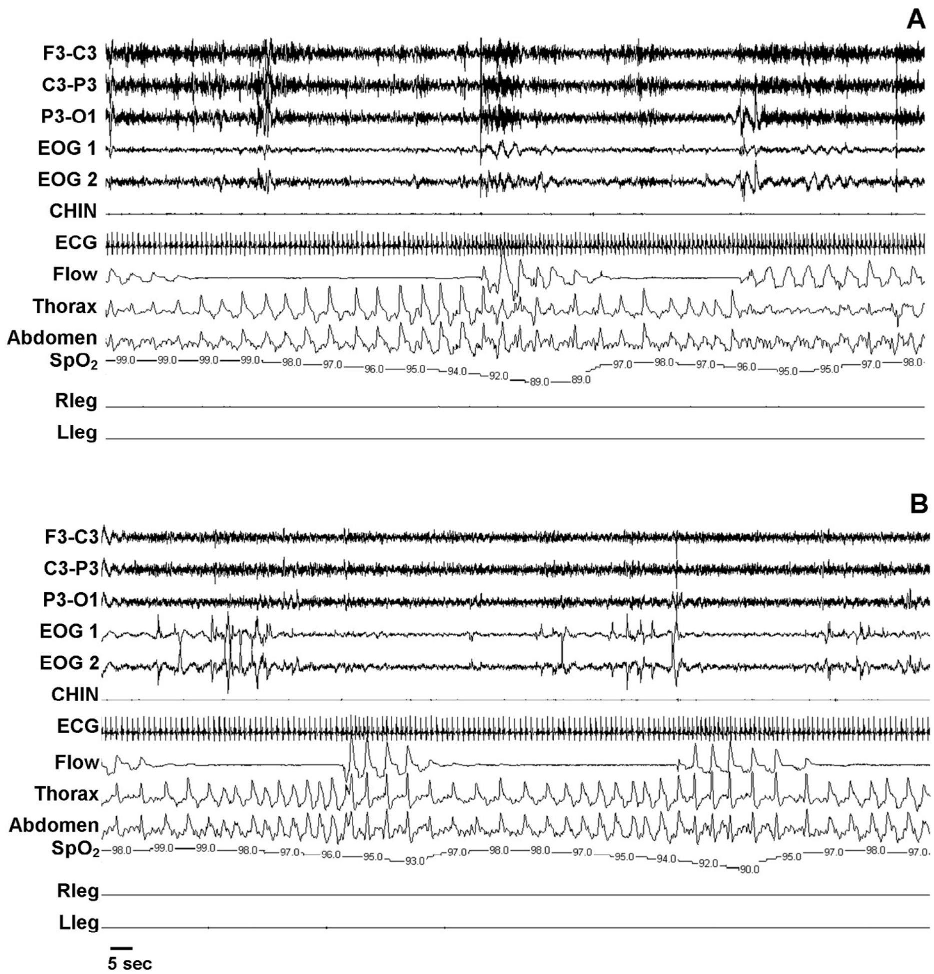

Fig. 1. Patient with a C5 lesion (ASIA A). Long obstructive sleep apnea occurring during both NREM (A) and REM (B) sleep associated with mild oxygen desaturations. EOG, electro-oculogram; ECG, electrocardiogram; Rleg, right tibial muscle; Lleg, left tibial muscle.

between airway dilator muscle and thoracic muscles [25]; elevated upper airway resistance due to decreased pharyngeal cross-sectional area related to sympathetic inhibition [26] in association with reduced lung volumes [27], and, finally, significant changes in compensatory reflex responses to ventilatory loading due to disrupted feedback afferents from rib cage receptors [28].

Moreover, considering that many SCI patients cannot change body position by themselves, the preferential adoption of a supine sleeping position, as observed in our patients, could impose increased gravitational stress upon the upper airway [6].

Independent from a diagnosis of SDB, 11 patients had an AHI ≥5 exclusively during REM sleep. Statistical analysis revealed that the occurrence of SDB exclusively during REM sleep was related to the presence of a complete motor lesion and to the age of the subject. Indeed, the presence of a complete motor lesion could further increase the physiologic reduction of intercostal and accessory muscle activity during REM sleep [29].

All of our patients with SDB showed an obstructive disorder, in agreement with previous studies [8,13]; however, central sleep apnea may occur in SCI due to the weakness of respiratory muscles or to the potential depressant effects of medication [8]. Only one of our patients showed nocturnal hypercapnia suggesting the presence of a sleep hypoventilation. Sleep hypoventilation is described in SCI patients and seems to be favored by the depressant effect of drugs, intercostal and abdominal muscle weakness and blunted ventilatory drive, especially in tetraplegic patients during REM sleep [11,30].

Finally, considering the severity of SDB, half of our subjects showed a mild disorder and in the majority of them obstructive sleep apnea events were frequently associated with mild desaturation (Fig. 1), as suggested by the mean of SpO_2 nadir value (89%). This observation, along with the finding that a conspicuous number of tetraplegic patients with SDB require significantly lower levels of CPAP pressures than able-bodied SDB subjects [31], suggests that other factors, different from the high airway collapse, might favor the occurrence of SDB [3].

The other main result of the present study concerns the presence and features of PLMS. Among SCI patients, the PLMS prevalence (28.6%) was higher than in the general Caucasian population (9.3%) [32]. We cannot exclude the presence of PLMS before the trauma. However, our population is composed of relatively young subjects, and PLMS generally occur after the age of 40 years [33]. Moreover, in the majority of patients, PLMS were present also during REM sleep and wakefulness. In the literature, little is known about PLMS in SCI subjects: a recent study, analyzing eight patients with complete chronic spinal cord lesions reports a PLMS prevalence of 37.5% [17]. Moreover, small case series described SCI patients with PLMS also during relaxed wakefulness [14] and REM sleep [14,15]. The mechanisms responsible for PLMS in SCI patients are incompletely understood. The high prevalence of PLMS in patients with complete spinal cord lesion and the presence of PLMS also during REM sleep and wakefulness seem to suggest the existence of a spinal cord central pattern generator of PLMS [15,17,34]. Such a spinal

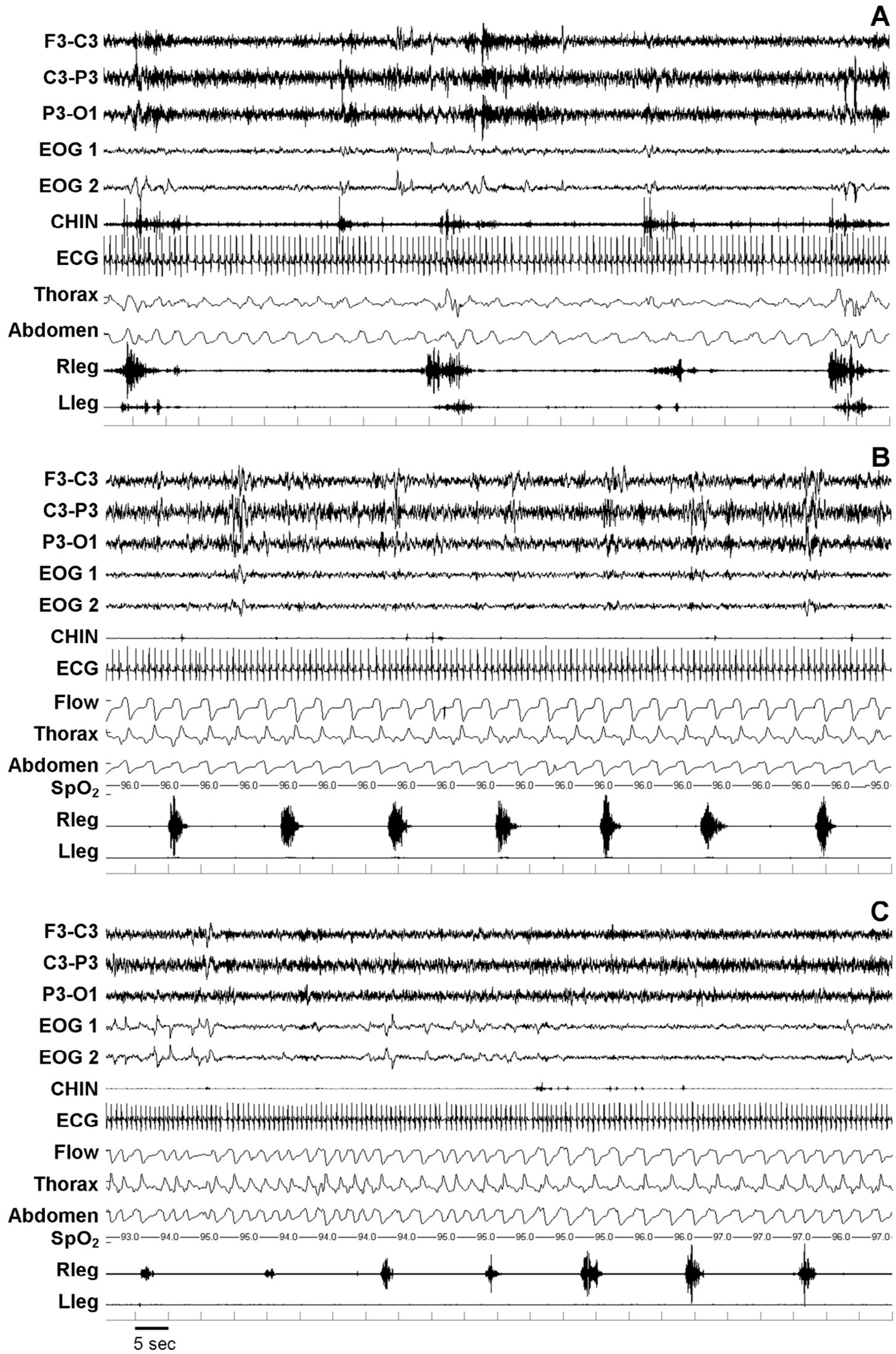

Fig. 2. Patient with a C4 lesion (ASIA C). Periodic leg movements occurring during wakefulness (A), NREM (B) and REM sleep (C). EOG, electro-oculogram; ECG, electrocardiogram; Rleg, right tibial muscle; Lleg, left tibial muscle.

generator would be released from the descending inhibitory supraspinal pathway [15,17,34]. Surprisingly, our statistical analysis revealed that PLMS were significantly more frequent in patients with an incomplete spinal cord lesion (50%) than in patients with a complete lesion (5.8%). More precisely only two patients with a complete motor lesion (one ASIA A and one ASIA B) presented PLMS.

As yet, there is no definitive explanation for this finding. To our knowledge, our study is the first to analyze PLMS in patients during the first year after SCI. We cannot exclude that patients with a complete lesion need more time to develop PLMS. Determining the time of onset and clinical evolution of PLMS following SCI might clarify this issue. Moreover, the analysis of the PLMS periodicity index [35] and the investigation of the relationships between PLM, cortical arousal and autonomic oscillations could help interpret this movement disorder in the context of SCI. A recent single case report suggests that PLMS can be disconnected from cortical arousals and not accompanied by autonomic modifications [36].

The main limitations of our study include the difficulty of interpreting standard sleep features and the presence of daytime sleepiness, as patients were assessed near the time of injury. Indeed,

especially during the initial phase of the hospitalization, when lack of daytime activity, depression, and pain are particularly disabling, SCI patients commonly show an irregular sleep–wake schedule that is further disturbed by frequent and long daytime naps. This condition precluded the adoption of a protocol to evaluate specific sleep parameters such as sleep latency or sleep efficiency. Nevertheless, a reduction of the percentage of REM sleep (<10% of total sleep time) was observed in 31.4% of our patients. Such a reduction did not seem to be related to the presence of respiratory or motor disturbances but was probably facilitated by medications. In the same vein, the assessment of excessive daytime sleepiness appeared particularly difficult in this group of patients. Indeed, although the Epworth Sleepiness Scale (ESS) [37] represents a standardized simple method for measuring the general level of daytime sleepiness, a number of situations described in ESS were not applicable to SCI patients (eg, car driving, outside visits). For this reason, we used a VAS and found only five patients complaining of daytime sleepiness. In none of these patients was sleepiness related to the presence of SDB or PLMS. Previous studies in SCI patients have confirmed the absence of an association between sleepiness and specific sleep disorders, such as SDB [8,11] or PLMS [17]. The cause of sleepiness in these patients is most probably multifactorial due to a combination of different factors such as fatigue, drugs, depression, and irregular sleep-wake schedule. It is interesting to notice that other patients, such as those with SDB and heart failure, seldom meet the criteria for subjective excessive daytime sleepiness. In these patients, the degree of subjective daytime sleepiness seems to be strictly influenced by the balance between the sympathetic and parasympathetic activity [38]. Further studies on the autonomic cardiac modulation could give insights for the comprehension of vigilance regulation in SCI patients.

Another methodological limitation of this study is the lack of a control group of normal healthy subjects matched for age, gender, and BMI. A future investigation should be conducted comparing the features of sleep disorders and their impact on sleep micro- and macro-structure in SCI patients and control population.

In conclusion, our study confirms the high prevalence of SDB and PLMS in SCI patients. By evaluating this population during the first year after the trauma, this study shows that independently from possible sub-acute and chronic clinical variables (weight gain, increase of abdominal or neck girth), the level and the completeness of the spinal cord lesion are the main factors associated, respectively, with early development of SDB and PLMS. The clinical impact, the long-term evolution and the efficacy of treatment of these sleep disorders in SCI patients will need to be assessed in future studies.

Funding

K.S. has received financial support from Vivisol s.r.l., SOL group.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.07.017.

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